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MAMMOGRAPHY SYSTEMS (BREAST CANCER)

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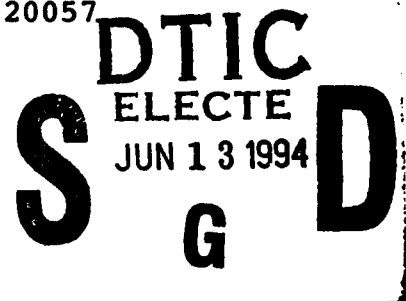
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## 13. ABSTRACT (Maximum 200 words)

Based on the work we have done this year, we believe that digital mammography using an existing commercial storage phosphor device combined with appropriate image processing does equal in phantoms the resolution of conventional screen film systems at an equivalent patient dose and can exceed the object detectability of conventional screen film systems when a higher patient dose is used.

During the optimization techniques, it also became apparent that some of the problems previously reported were secondary to static electrical charges and dust. We found it essential to be unusually careful in controlling dust to avoid calcium like artifacts. The preliminary studies suggest that the use of a 35 micron film digitizer coupled with appropriate image processing may allow the replacement of direct geometric magnification with electronic magnification. With electronic magnification, the conventional screen film image is digitized at 35 microns. A small section of this is then displayed as an enlarged image. With appropriate image processing, it is possible to see calcifications and details in shapes of calcifications that cannot be seen either directly or with a magnifying glass on the original image. Our experiments suggest that film digitization with very small pixel sizes may prove to be a viable method for digital mammography. We will be continuing our research with a 42 micron film digitizer when a machine arrives at our site early in 1994.

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## **ENHANCEMENT OF CURRENT TECHNOLOGIES FOR DIGITAL MAMMOGRAPHY**

### **1.0 INTRODUCTION:**

The first year of the project was spent gathering preliminary data essential to understanding the requirements for digital mammography in two areas: image acquisition, and electronic image processing using two existing technologies, film scanner and storage phosphore plate system. There are almost no publications in this field relevant to the specific work done in this project. There are related publications in chest imaging and these will be referred to as indicated.

Although digital mammography is in limited clinical use in Europe (1,2,3,4), it is still considered an experimental technique in the United States where it has been described as being promising, but not having sufficient resolution (4,5,6) or of insufficient resolution with the possibility of improved resolution far in the future (7). Based on our experiments in system optimization, we believe we understand the disagreement in opinions is likely due either to differences in exposure factors used or differences in the image processing parameters used by different centers. Unfortunately, the actual image processing parameters used by various authors and the actual exposures used are usually not mentioned in these articles, but as our work suggests, the appropriate setting of these factors is essential to high quality digital mammography.

Based on the work we have done this year, we believe that digital mammography using an existing commercial storage phosphor device combined with appropriate image processing does equal in phantoms the resolution of conventional screen film systems at an equivalent patient dose and can exceed the object detectability of conventional screen film systems when a higher patient dose is used. To achieve these results, however, it was necessary to use different image processing methods than those recommended by the manufacturer. These more optimal image processing methods were derived from optimization response surface experiments performed this year. The method used to arrive at the more optimal image processing settings was derived from the methods used for image optimization that we previously used with AGFA's CR system and Fuji CR's used for chest and bone images that we previously reported. (8,9)

During the optimization techniques, it also became apparent those some of the problems previously reported were secondary to static electrical charges and dust. We found it essential to be unusually careful in controlling dust to avoid calcium like artifacts.

The narrative summary that follows is based on individual experiments that are briefly described in the appendix. In this narrative, they are referred to by the number given them in the Appendix A.

## **2.0 THE ASSIGNED TASKS FOR THIS PROJECT ARE:**

1. Evaluate the current status of existing digital mammography systems for direct digital mammography and film digitization.
2. Develop a strategy for the optimization of these existing systems including optimization of KVP and MAS.
3. Compare the accuracy of these existing systems to conventional screen film systems if the systems appear to be adequate replacements for existing screen film systems using ROC methodology
4. Provide recommendations about how these systems could be implemented to replace existing screen film mammography.

## **3.0 THE THREE COMPONENTS FOR SUCCESSFUL DIGITAL MAMMOGRAPHY:**

There are three components required for the successful development of a digital mammography system. These are the methods of image acquisition, the methods of image processing, and the methods for image display. This research deals primarily about the first two factors and image display is handled in a more comprehensive manner in a separate but related project. The research from the first year has demonstrated the requirements for image acquisition and has demonstrated appropriate parameters for portions of the necessary image processing. Image display is also discussed.

This report will take each of the areas in turn, define initial state of knowledge, summarize the results of the research done by our team, and indicate the relevance of this work to the final project aims.

## **4.0 IMAGE ACQUISITION FOR DIGITAL MAMMOGRAPHY**

### **4.1 Initial state of knowledge:**

#### **Relevant Prior Publications:**

Publications on digital mammography implied that the development of a digital mammography system would require the development of new detectors because existing systems did not have adequate resolution. (4,5,6,7)

We could find no articles specifying the required resolution for digital mammography. There are a few articles describing that 100 micron pixel size appears not to be sufficient. One source (7) suggested specific resolutions were based on the assumption that it should equal the high contrast resolution of screen-film mammography: 20 line pairs per mm.

Oestmann (10) reporting work with a 5 lp/mm storage phosphor system reported that while a 5 lp/mm system was sufficient to detect all clusters of microcalcifications, that individual microcalcifications were less well seen at this resolution. He reports that he selected image processing settings that resulted in images "similar to those of conventional mammography." He used the same exposure as used for the conventional screen film images he obtained for comparison (30 KVP at 250 mAs). This is a higher KVP than would

normally be used for conventional mammography and would be expected to decrease the contrast of calcifications on the conventional images (our most common setting is 26 KVP).

Chan (11) reporting on the use of high quality film digitization at 100 micron pixel size found that digitized mammograms provided lower detectability of subtle microcalcifications than conventional screen film mammography. She found that unsharp masking improved the detectability of the calcifications, but that even with unsharp masking, the conventional screen film mammograms still had a higher detectability rate. She indicates that this is due to their being a higher false positive rate.

#### **4.3 Exposure:**

We assumed that any system developed would have to use the same or less exposure than conventional screen-film mammography.

#### **4.4 Methods of obtaining a digital mammogram:**

There are two methods of creating a digital mammogram: direct digital acquisition and digital transformation of an analog image. Direct digital mammography systems either existing or under development use storage phosphor plates, charged coupled devices (CCD), selenium plates or electron capture devices. Film digitization devices can be based on laser, monochromatic or diffuse light.

##### **4.4.1 Direct Digital Mammography Devices:**

A survey of existing direct digital mammography machines revealed that only Fuji Corporation had a working FDA approved system for digital mammography. We acquired such a system for testing in September, 1993. No other existing commercial machine was identified. Research devices are under development by Dr. Martin Yaffee in Toronto, by Lorad Corporation, 3M, and by Fischer Corporation in the U.S. and Fuji Corporation in Japan. In addition, several smaller companies are exploring various devices. These include Photometrics and Princeton Instruments. We are working with 3M and with Princeton Instruments on their machines and have had discussions with Photometrics, Lorad and others. These devices are not yet finished and were unavailable for testing. Images from some of these machines have been reviewed. Currently the Lorad images are the most promising, but we were unable to do a true assessment of the machine.



#### **4.4.2 Film Digitization for Digital Mammography:**

There are existing devices for film digitization based on laser or CCD technology using 100 to 200 micron pixel sizes available from multiple vendors including Lumisys, Vidor, Vision 10, and others. There are a few companies claiming 50 micron digitization capabilities, usually over a limited range of optical densities. We have been investigating the technology under development by DBA, Inc. This 42 micron pixel system has had construction delays and should be delivered to us in January, 1994, for intensive testing. Should film digitization prove to be an appropriate technology for further investigation, then the required pixel size for this technology could be determined. Tests to determine the preferred contrast characteristics for mammograms to be digitized will be determined once the machine is on site.

#### **4.5 An Evaluation of the Resolution Requirements for Digital Mammography:**

At the start of this project, we could find no information related to the pixel size that a digital mammography machine would have to have to equal the detectability of objects seen on screen-film mammography. The two articles mentioned above (Oestmann and Chan) suggested that 100 micron pixel size was insufficient. Screen-film mammography systems can have up to 20 line pairs per millimeter (lp/mm) of high contrast resolution. This would imply that one would need a system with 25 micron pixel size to equal the high contrast resolution of screen-film. The only contemplated systems that we are aware of that come close to this resolution are film scanners. If indeed this resolution was required, then all of the direct digital systems under development would end up being insufficient for digital mammography. Because of this we undertook both an experimental and theoretical approach to determine the effect of different pixel sizes on the detection of very small radiodense objects. The theory will be presented first followed by the experimental evidence that supports it. This will then be followed by a discussion of the implications of these findings for further research. (This material was presented at the Computer Assisted Radiology (CAR) Meeting in Berlin, June, 1994.)

##### **4.5.1 Theoretical Approach to determining the pixel size needed to detect a small object of specified size:**

###### **Definitions:**

A small object is an object close to the size of the pixel. They are assumed to be spherical and of calcium radiodensity.

Pixels are assumed to be square.

Voxels are rectangular solids that contain all the region from the x-ray tube to the region that project onto the pixel.

The detector is assumed to be a storage phosphor imaging plate with inherent light scattering potential.

The focal spot size is small, but finite; therefore an object being imaged casts a penumbra (or shadow).

#### 4.5.1.1 FILLING THE PIXEL:

It order to obtain maximal information from a pixel, the process being evaluated should completely fill the pixel. Because microcalcifications are assumed to be spherical, the minimum detectable size is greater than the pixel diameter. In actual appearance, the microcalcifications are irregular, but closer in shape to a sphere than a cube. The diagram demonstrates the necessary size..

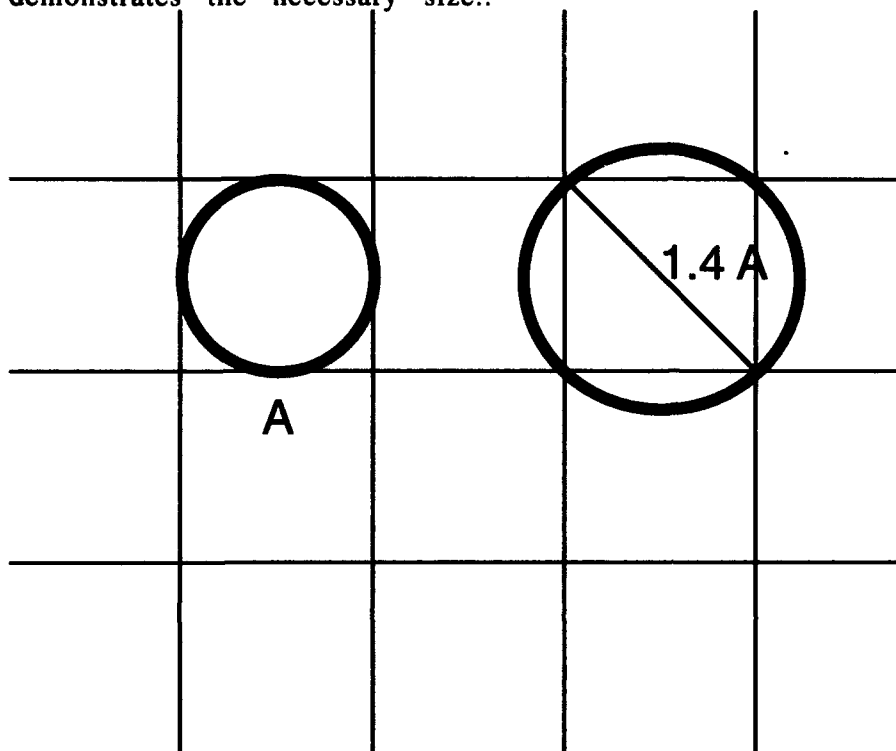


Figure 1: A sphere within a pixel has the same diameter as the pixel, but fills only 50% a cubic voxel of the same size. To fill a pixel of size A, need a sphere, if centered on pixel of size A, by Pythagorean Theorem:  $A\sqrt{2}$ .

#### 4.5.1.2 EFFECT IF OBJECT IS NOT CENTERED TO PIXEL

If the spherical calcium object is not centered to the pixel, then the offset will result in less of the pixel being filled. If calcium is  $\sqrt{2} A$ , minimum density will be 1/4 of that if pixel completely filled. (37% filled, but because of sphere only 1/4 of density) as shown in Figures 2 and 4.

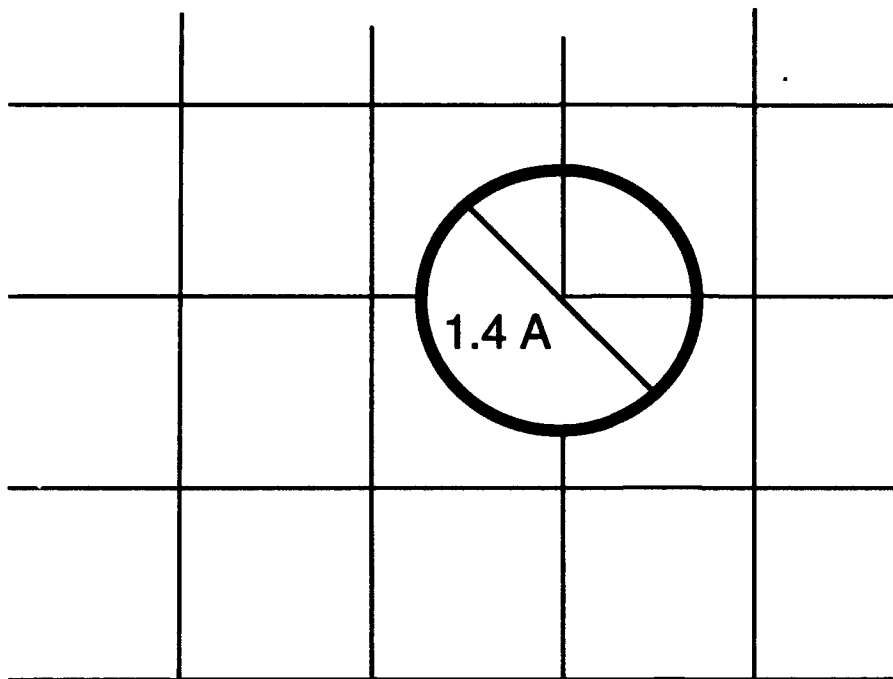


Figure 2: Drawing showing effect of maximal offset of  $\sqrt{2} A$  sphere on area of pixel filled.

This positioning does not appear to be sufficient contrast to be detectable in experimental tests.

If offset maximal amount (oblique)  
 need  $2A\sqrt{2}$  to be certain that at least one pixel is completely filled.

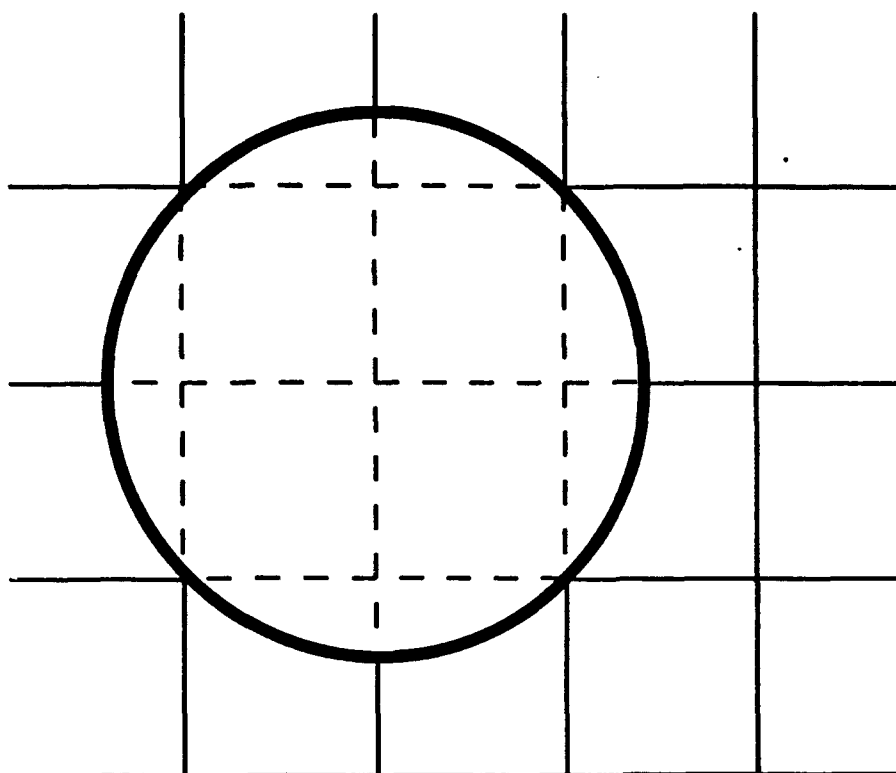


Figure 3: Drawing of sphere of diameter  $2A\sqrt{2}$  offset to corner of pixel.

Therefore in order to see a small calcific object with a detector with pixel size  $A$ , one needs a  $2A\sqrt{2}$  sized object. This hypothesis is supported by our experimental evidence.

Standard sized objects on mammographic phantoms are at 160, 240, and 320 microns. In order to see a

320 micron object need	114 micron pixel
240 micron object need	85 micron pixel
160 micron object need	57 micron pixel

On the phantom used for American College of Radiology certification, one needs to see the 320 micron objects and some screen-film systems allow detection of 240 micron objects at least part of the time. Thus to equal screen-film one should be aiming either for a 114 micron or an 85 micron pixel size.

#### 4.5.1.3. FILLING THE PIXEL: EXPERIMENTAL EVIDENCE

In the actual experiments (experiments listed in appendix as I-A), one does slightly better than this because the focal spot size is finite and therefore there is a penumbra around the small object enlarging its projected size. Thus, in tests, we can just faintly see the 160 micron object with 83 micron pixel. While this suggests that one may need only  $2A$ , rather than  $2A\sqrt{2}$  to see object given contrast enhancement possible with image processing, actual measurements of the objects in the phantom indicate that as projected onto conventional screen film systems, that the objects and their penumbra are actually larger. This is shown in the following table:

## MEASURED ALUMINUM SPECKS IN "ACR" PHANTOM

STANDARD	INSERT ONLY		COMPLETE	
	SF	SR	SF	SR
540:	650	650	700	700
400:	600	600	650	650
320:	350	450	400	450

In microns

SF = Screen Film Image

SR = Storage Phosphor Image

Differences due in part to magnification, Penumbra

## MEASURED OBJECTS IN CIRS DETAIL PHANTOM

Calcium flecks in microns

Standard	Screen-Film SR		SR 1.5 X
390	700	700	1000+
270	500	500	800
230	400	400	600
200	300	350	500
160			300

Thus, these measurements suggest that the actual projected size of the 200 micron flecks seen on the CIRS phantom with a 100 micron pixel size are really 300 microns and the 160 micron aluminum hydroxide flecks seen on the RMI phantom with an 83 micron equivalent pixel are really probably about 200 microns supporting the theoretical model of a pixel of size  $A$  can detect a calcium object  $2 A \sqrt{2}$ .

### 4.5.1.4 MEASURED SIZE OF CALCIFICATIONS IN BREAST BIOPSY SPECIMENS

Measurements using an 8 X magnifier and measuring reticle demonstrated that in 10 contact specimen biopsies radiographs (20 line pair system) that most of the calcifications that could be resolved as individual objects measured 300-600 microns. There were some 200 micron calcifications that could be individually identified, and then there were areas of calcification with particles that could not be resolved. Since this tested system has less noise, less scatter and less penumbra than any conventional screen film mammogram could have, we believe that the lower limit of size that we need to resolve for clinical purposes is 200 microns.

### 4.5.1.5 EFFECT OF NOT FILLING PIXEL

To better understand the implications of this model, it is helpful to understand the implications of failure of the projected object to completely fill the pixel. The effect is analogous to the partial volume effect seen with computed tomography. One sees decreased contrast.

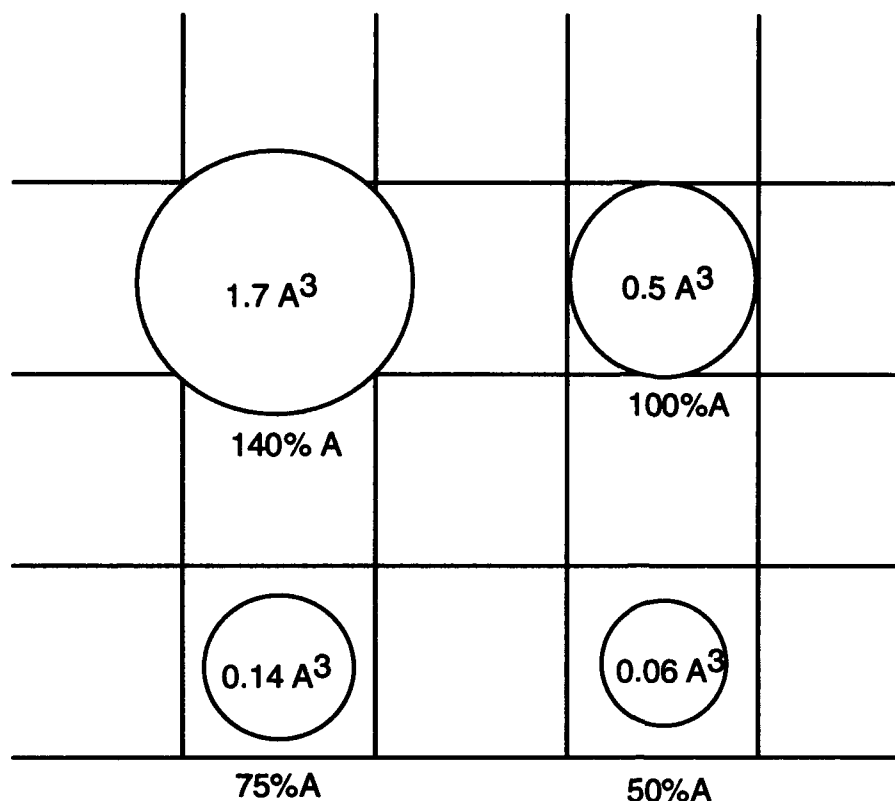


Figure 4: The volume of calcium projected in sphere of pixel size A with spheres of different sizes projected in center of pixel. (Based on solid geometry formulas.)

There is a rapid decrease in density when sphere is smaller than pixel size.

#### 4.5.2 IMPLICATIONS OF THIS HYPOTHESIS:

##### 4.5.2.1. The Direct Hit Phenomenon:

In this model we have assumed that the shadow from the calcium fleck will be maximally offset from the center of the pixel. In actual practice one would expect that intermittently, the shadow would fall directly on the center of a pixel and thus one could occasionally see a calcium object that is the size of the pixel (assuming that the calcium object and its penumbra completely fill the pixel. Calcium flecks intermediate in size between pixel size and  $2 A \sqrt{2}$  have an increasing chance of having their shadow projected directly over a pixel with the likelihood increasing as the size of the calcium fleck increases. The formula  $2 A \sqrt{2}$  is the size necessary to assure visualization.

##### 4.5.2.2. The increased radiodensity phenomenon:

We have confirmed the model using calcium or aluminum hydroxide flecks in the phantom. Objects of increased radiodensity can be seen at smaller sizes. We found using the CDMAM phantom (Nuclear Associates) (experiments listed in appendix as IV-A-1) that an object that is visible at 320 micron diameter and thickness can also be seen with a 100 micron pixel. When the thickness is 1000 microns, its diameter need only be 130 microns. (if one offset an object  $A \sqrt{2}$  times the pixel size by its maximal amount, it would fill 37% of the volume that would be filled if it were centered on the pixel. Thus the theory holds approximately.

The clinical applicability of this is that when there are malignancy associated calcifications, there are often many of them and they may be superimposed on each other, and thus visible at a smaller size. While this will help in many cancers, there are cancers with only a few calcifications. These will not have superimposed calcifications and will not demonstrate this phenomenon.

#### **4.5.2.3. The signal to noise phenomenon:**

This model is based on a receptor with a signal to noise ratio of the Fuji storage phosphor imaging plates and plate reader. The system in our experiments is noise limited. In our experiments, increasing the exposure to improve the signal to noise ratio improves the detectability of small objects. (experiments listed in appendix as IV-D) Therefore anything done to improve the signal to noise ratio will decrease the minimum size detectability: either better electronics or better receptors.

#### **4.5.2.4 IMPLICATIONS FOR DIFFERENTIATING DUST PARTICLES FROM TRUE MICROCALCIFICATIONS**

In our initial experiments we found that the digital system had many calcium fleck like artifacts. Because we believed these to be dust, we investigated the appearance of dust particles on storage phosphor systems. We found two effects: (1) dust reflected more light than is normally emitted by the phosphor screen, resulting in a high signal to noise ratio spot; (2) dust prevented the erasure of regions under dust particles resulting in a black spot on the subsequent image.

The high signal to noise ratio induced by the reflection of dust particles means that they can be seen at a smaller size than true areas of decreased light emission that result from the shadow cast by a true microcalcification. Thus it becomes possible to correctly differentiate some dust particles from true microcalcifications. Easily seen objects close to 1 pixel diameter in size are usually dust particles and should not be confused with microcalcifications.

Larger dust particles can be confused with microcalcifications and therefore one must keep the digital system unusually clean. Unlike dust in a screen-film system where the dust interferes with the exposure of the film and therefore creates an unusually bright, sharp edged defect, dust on a phosphor plate tends to result in an image that is not very different in brightness or edge characteristics from that of a true calcium particle.

#### **4.5.2.5 IMPLICATIONS RELATED TO CHARACTERISTICS OF POTENTIAL DIRECT DIGITAL DETECTORS:**

For systems with a signal to noise ratio at standard mammographic exposures similar to that of Fuji's storage phosphor imaging plates and plate reader lasers and electronics, one should consider 114 to 85 microns as the desired maximal pixel size.

One could expect to improve the detectability of small objects either by decreasing pixel size or improving signal to noise ratio.

One could decrease the effective pixel size either by developing a device with a smaller pixel or by using direct geometric magnification onto a receptor with a larger pixel size than optimally desired. (experiments listed in appendix as I-A,B,C,D) Advantages of using direct geometric magnification are that one may be able to use a receptor with higher radiation sensitivity than the high resolution systems provide, thus decreasing

patient dose. One could also use existing detectors without having to develop new detector systems. The disadvantages of using direct geometric magnification are that at least some current mammographic units do not have enough spread of the x-ray beam through the built in collimator to cover the whole breast in the magnification mode. Also the focal spot size of the x-ray tube would result in a larger penumbra around the actual object. There is also the potential for this system to exaggerate motion unsharpness by inadvertent patient motion.

One could improve signal to noise ratio either by having improved detectors or by accepting an increase in exposure. Our experiments demonstrate that an increased exposure does result in smaller objects being seen. (experiments listed in appendix as IV-A,D)

#### **4.6 THE POTENTIAL FOR DECREASING EXPOSURE USING DIGITAL SYSTEMS:**

In our tests, we found that the Fuji high resolution plates appeared to require the same exposure as our standard screen-film system for the demonstration of equal information. In the experiment (experiments listed in appendix as IV-A-1,2,3,4) that we did comparing the effect of decreased exposure on detectability of objects in the CDMAM phantom, we found at the lowest exposure level we tested, that the digital system performed better than the screen-film system, but we found in a small sample that only 1 of 20 of our cases had any region in the breast with such a low exposure and that these regions were clinically underexposed. Once we exceeded this minimal exposure, the screen film system performed better. This was an early experiment before we had reached our current knowledge of image processing, and will need to be reevaluated. Our preliminary data suggests however that there will be no potential decrease in exposure possible, unless one is willing to work with less information than screen film systems provide.

Other work in which we did direct geometric magnification onto a standard phosphor plate demonstrated that with appropriate image processing, that one could see more on magnification views with a lower exposure than on magnification views recorded on screen film systems. (experiments listed in appendix as I-B) This suggests that one should evaluate the value of doing geometric magnification views onto higher sensitivity, but lower resolution film than is used for standard mammography. Other work done elsewhere suggests that there may be value in using direct geometric magnification on all mammograms.

#### **4.7 FILM DIGITIZATION:**

Work done in our labs (experiments listed in appendix as II-A) indicated that film digitization at 170 microns was insufficient to allow detection of smaller microcalcifications. Work done by Chan (11) has indicated that 100 microns is either just sufficient or just insufficient for detection of microcalcifications.

We have done a limited amount of investigation of an experimental 35 micron film digitizer at the manufacturers office. Our experiments (experiments listed in appendix as II-B) with this device suggest that there may be some value to using film digitization for digital mammography. A version of this device will be placed at Georgetown shortly and next years report will detail our results more fully.

The preliminary studies suggest that the use of a 35 micron film digitizer coupled with appropriate image processing may allow the replacement of direct geometric magnification with electronic magnification. (12) With electronic magnification, the



conventional screen film image is digitized at 35 microns. A small section of this is then displayed as an enlarged image. With appropriate image processing, it is possible to see calcifications and details in shapes of calcifications that cannot be seen either directly or with a magnifying glass on the original image.

The benefit does not appear to come from the magnification, since the type of hand held magnifier commonly used by radiologists when they interpret screen film mammography is sufficient to detect 30+ line pairs per mm of high contrast detail. The benefit appears to result from the image processing that allows improvements in object contrast that occur from gray scale changes and edge enhancement. Our experiments suggest that film digitization with very small pixel sizes may prove to be a viable method for digital mammography.

We will be continuing our research with a 42 micron film digitizer when a machine arrives at our site early in 1994.

## **5.0 IMAGE PROCESSING:**

Image processing is the second major component of digital mammography. Correct image processing enhances the ability to see abnormalities in digital images. Incorrect image processing can conceal information. There have been a few publications on optimizing image processing in chest images including several of our own, but we are not aware of publications on optimizing image processing in digital mammography. We presented our preliminary material at the annual Meeting of the Radiologic Society of North American in December 1994. (13) We will be presenting this material at the meeting of the Society of Photo-optical instrumentation Engineers (SPIE) in February, 1994 and this report will be published as part of their Proceedings. Apart from our own work in image processing in digital mammography and limited work done by Chan (11) on digitized film images, we are unaware of any reports of similar work.

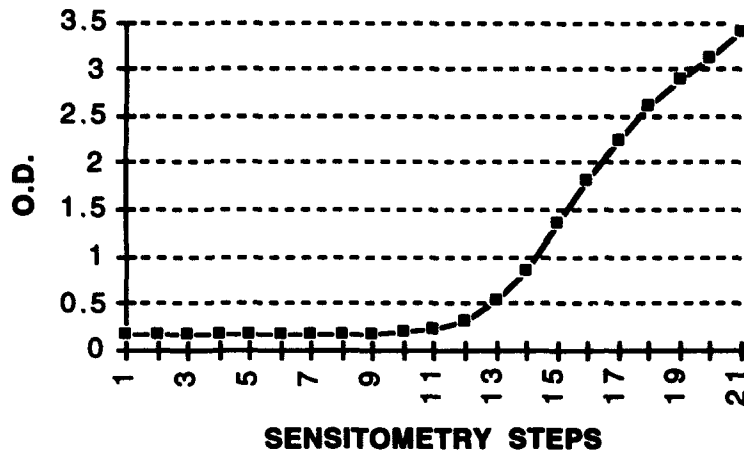
### **5.1 The Types of Image Processing:**

Image processing as currently available consists of three main potential changes in the image. These are changes in the look up table (LUT) to affect optical density and contrast, changes in spatial frequency to effect either edge enhancement or noise reduction, and methods for balancing the optical density in an image (often called histogram equalization) in order to better match the original information to the characteristics of the display device used. Each of these provides an important advantage to diagnosing breast cancer on digital mammography. Image processing can be used on any digital mammographic image, independent of the method used for acquiring the digital image. The techniques are the same for different digital detectors and for both direct digital and film digitization methods.

#### **5.1.1 CHANGES IN LOOK UP TABLE:**

Changes in the look up table change the way in which the acquired information which is related to the exposure received by the imaging plate is mapped to a specific optical density or luminance on the display device. This mapping is important because the original receptor may be linear or non linear in its response and all current display devices are non-linear, but differ in their non-linear response characteristics. If one considers only the display devices, for the moment, the response characteristics are characterized by a non-linear S-shaped curve. This curve, well described for film as the H and D or characteristic curve is also reflected in the pattern of display seen in the luminance values on monitors (14).

## H AND D FUJI MAMMOGRAPHIC FILM



The characteristic curve is S-Shaped and is usually divided into three sections for discussion purposes: The toe, the shoulder and the central portion. The contrast in the toe (bottom) and shoulder (top) of the curve is less than that in the central portion of the curve. For digital mammography, the most important regions are the toe (the region of low exposure) and the central portion (where the highest contrast is). The dense breast is one in which there is a large amount of tissue that is close to the density of calcium. If this region of breast density is mapped into the toe region of the characteristic curve, then all structures in that region will be of lower contrast. If the calcifications are projected in a region of increased breast radiodensity, then they will be of low contrast compared to the background tissue and therefore more difficult to see. The application of changes in the LUT to change the final optical density and contrast are to change the optical density of the region where calcium could be partially obscured by shifting densities to the region above the toe of the characteristic curve and to increase the slope of the characteristic curve in regions of increased breast radiodensity.

In our evaluation of changes in the LUT (experiments listed in appendix as IV-A-1,2,3,4,B,C), we recorded the characteristic curve of the screen film system used for our current mammography, a second screen film system and then measured the optical density of mammograms in our collection at the sites where cancer had been found. In 1 of the 20 measured, the microcalcifications associated with the cancer were in a region where the optical density of the region of that breast was in the low contrast region of the toe of the characteristic curve. Thus a simple remapping of the optical density to a region above the toe of the characteristic curve would have improved the detectability of the calcifications in 5% of this small sample. A second experiment in which we changed the LUT of a digital image of the CDMAM phantom so that it was printed at different optical densities confirmed that at low OD, there was less detectability of objects, but that once one was above the toe of the characteristic curve, the detection rate did not change over a wide range of OD values.

Increasing the contrast in the steepest portion of the characteristic curve should also help in the detection of microcalcifications. Our preliminary tests suggest that there is

a limited range of this effect from a contrast value of roughly  $GA = 0.8$  to  $GA = 2.5$ . Above and below this range, the detectability decreased. Within this range our preliminary results detected no change. Above  $GA = 2.5$ , the accentuation of noise limited the visibility of objects in the image of the phantom.

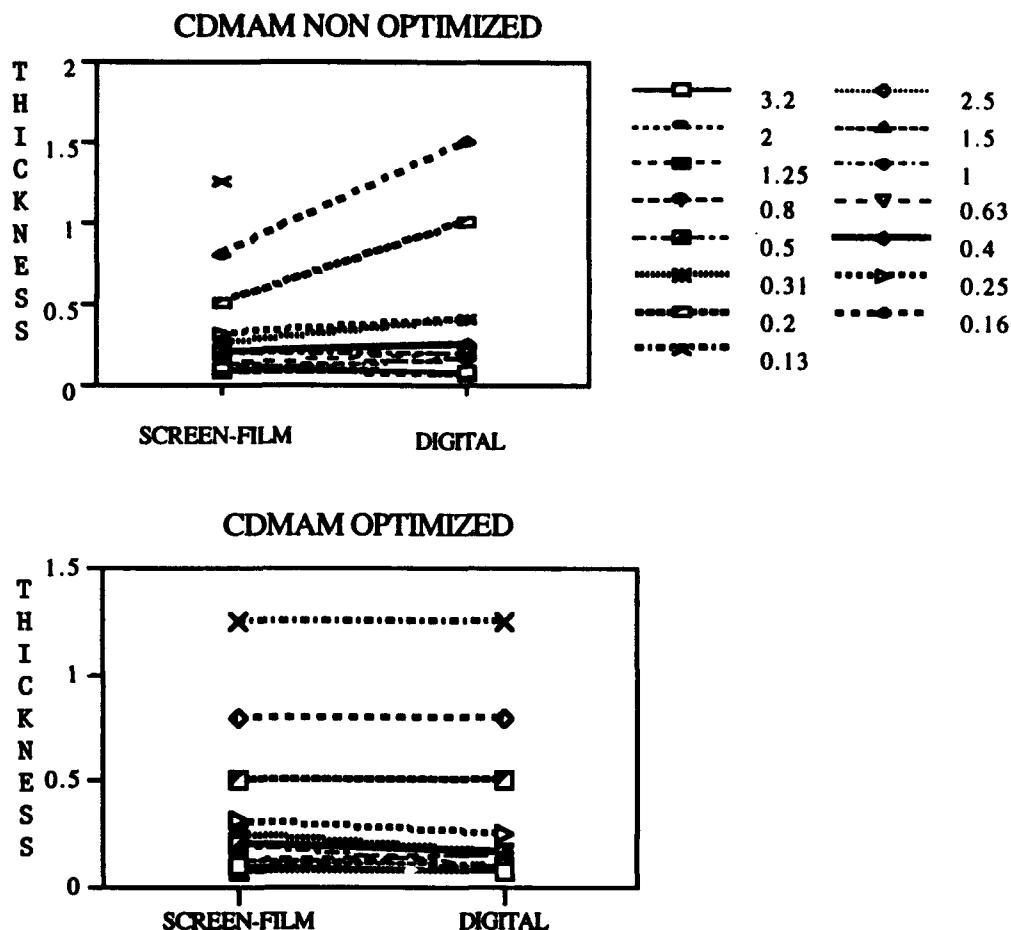
### 5.1.2 SPATIAL FREQUENCY CHANGES:

All images are composed of a combination of many spatial frequencies. High spatial frequencies correspond to sharp edges. Low spatial frequencies correspond to smooth edges. Several methods exist for altering the spatial frequency patterns within an image. Our work was done with a method called unsharp masking using a convolution kernel of various sizes. In this method, a kernel representing an array of numbers is multiplied by the pixel values in the image changing its final appearance. The method used was that of Fuji in which kernels of different sizes are named as settings of an RN factor and vary from 0 to 9. The emphasis given to this spatial frequency effect is named the RE factor and varies from 0 to 16. In addition there is an additional effect acting on the image only in regions of low optical density called the RT factor. The RT factor is used to decrease the visibility of noise at low exposure/low optical density regions of the image.

We tested various combinations of RN, RT, and RE settings in mammography phantoms. (experiments listed in appendix as IV-E) Our results indicate that the detection of microcalcifications is improved by small kernel sizes and by intermediate to high settings of frequency enhancement. Larger kernel sizes aided in the detection of small masses. None of the factors tested had much effect on the detection of fibers. Because the best detection of microcalcifications occurred with the smallest kernel size, it is possible that a still smaller kernel size could offer additional improvement. We found that certain of the settings, especially those with a larger kernel size or with a large amount of spatial frequency emphasis improved the detectability of objects in mammographic phantoms, but resulted in digitally obtained breast images that were sufficiently unusual in appearance that they would likely be rejected by radiologists. A setting that best demonstrated small masses could also obscure microcalcifications and visa versa. (experiments listed in appendix as IV-F)

Based on our preliminary data we now consider that settings of  $GA = 1.5$ ,  $RN = 9$ ,  $RE = 5$  to be a partially optimized set of values for image processing of digital mammography.

The effect of this setting is shown in the two graphs below. In the first, the image processing setting recommended by Fuji for digital mammograms is used. For all small objects, the screen film system performs better. In the second graph, the change in image processing following our optimization procedure indicates that with proper image processing, screen film and digital mammography show equal detectability of objects on the CDMAM phantom.



### 5.1.3 OPTICAL DENSITY ADJUSTMENT METHODS:

The range of radiodensities in the breast is wide and their distribution is unequal. On conventional screen film mammography it is difficult to have adequate contrast in the more radiodense regions of the breast and still have sufficient range of visible densities to adequately see the skin thickness. There are available methods for adjusting the range of optical densities within a final image that allow different optical density regions to have different LUT. These methods, sometimes called histogram equalization methods could be useful in the display of digital mammography. In late December, 1993, we had such an investigational device implemented on the Fuji system we use for digital mammography. We will be investigating the effect of this in 1994.

## 6.0 IMAGE DISPLAY

Image display is an essential part of digital mammography. Conventional screen film mammography allows the display of 20 lp/mm of high contrast information. At the lower contrast range in which mammography falls, however, it is somewhere between 2.5 to 5 lp/mm actual resolution. Conventional breast images are most often 8 x 10 inches, but in about 10% of cases, 10 x 12 images are produced.

There are two potential methods for the display of digital mammography: Display on workstations and display on laser prints. These two methods for display of

digital mammograms are limited in their capabilities and new methods are unlikely to emerge in the near future.

When one displays digital information, the display can be of different sizes. One therefore has to consider the number of pixels in the total display as well as their spacing. Using a larger monitor does not increase the number of pixels displayed, but may display them at a size that is easier to interpret due to the magnification resulting from the larger display. With laser camera prints, the limit is 300 dots per inch. The larger the film, the more pixels that can theoretically be displayed.

## **6.1 Pixel Size and Number Related Factors:**

### **6.1.1 Display on a Workstation:**

The highest pixel number available on workstation monitors is 2,048 x 2500 pixels. If one is projecting an image of the breast originally obtained on an 8 x 10 inch receptor, this implies that one would be limited to displaying 100 micron data if one wished to display the entire image at one time. As indicated above, this would result in an image that would approximately equal the image of screen film mammography.

If one captured the data at a smaller pixel size, one could not display the entire image at this higher pixel size, but would have to scan through the image region by region magnifying each section of the image to assure detection of microcalcifications.

### **6.1.2 Display on a Laser Print:**

Laser print systems are currently limited to 300 dots per inch (DPI). If one is using 14 x 17 inch film, this is equivalent to approximately 4,000 x 5,000 pixels. Thus one could display a single breast at a size of 14 x 17 inches and thus display an image that used a 50 micron pixel on an originally sized 8 x 10 inch image. If one chose to display the image close to its original size of 8 x 10 inches, then one would be able to display the whole image with only 100 micron resolution.

## **6.2 The Effect of Image Display Size:**

The effects of image display size are different for monitors and laser film prints.

### **6.2.1 Display on a workstation monitor:**

Workstation monitors are limited to approximately 2000 x 2500 pixels. As one changes the size of the monitor, the number of pixels remains the same, but the size of each pixel in the display changes. When radiologists interpret screen film mammography, they usually use a magnifying lens to magnify the microcalcifications to make them more apparent. Typical magnification glasses used are 2 X or 3 X magnifiers. The use of such a magnifier allows as much as 30 line pairs of high contrast detail to be seen based on tests. Thus this use of a magnifier lens exceeds the high contrast resolution of screen film mammography. The best display size for digital mammograms is yet to be determined. Based on the measurements made with the hand magnifier, we will test monitors of different sizes in 1994 using

monitor displays of different sizes using image processing optimized images of breast phantoms. Our hypothesis is that displaying the image at 1.5 X normal size (12 x 15 inches) will likely provide full benefit, but we will also test larger sized monitors.

#### **6.2.2 Display as a laser print:**

Current laser print technology is limited to 300 dots per inch (dpi). According to our industrial sources higher resolution systems are not likely to be developed in the near future. There are at least two different methods of positioning information within each of the dots: the standard half-tone method and the Scitex patented method which divides each dot into multiple smaller dots for printing purposes. (15) The Scitex method currently only prints on paper, but appears to give a visually smoother image than halftone methods meaning that the edges of pixels are less apparent on image magnification. We are working with Scitex to test their system for the display of digital mammography.

With laser technology limited to 300 dpi, the choice of the desired resolution affects the final image display size. Currently, these have a maximal 4096 x 5000 in 14 x 17 inches. This means that each pixel in the final image is approximately 86 microns in size. If one starts with an 8 x 10 inch image of the breast and divides that image into 4000 x 5000 pixels, then each original pixel is 50 microns. Thus one can display a 50 micron image with slight magnification on a 14 x 17 laser print.

The effect of such a large image on the interpretive abilities of radiologists is not known to us. This would need to be tested.

### **7.0 COORDINATION OF RESEARCH WITH MILITARY MEDICAL CENTERS**

Coordination of the research projects with radiologists at Madigan Army Medical Center (MAMC) and Brooke Army Medical Center (BAMC) has been underway since the award of the contract. Face to face discussions have been held with Col Sam Babu, M.D. and Major Donald Smith, M.D. at MAMC and with Col Anna Chacko, M.D., Major Michael Cawthon, M.D., and Major Robert Shah, M.D. at BAMC. Direct coordination of the projects will be with Majors Shah and Smith. Currently, these two have been kept informed of our progress in digital mammography and are collecting cases for film digitization for incorporation into the research project. Once the digital systems are ready for clinical tests, detailed planning sessions will be held with them regarding research design and the implementation of the ROC studies will be done jointly at MAMC, BAMC, and Georgetown.

Evidence of our ability to work in a collaborative relationship with the DoD is demonstrated in the attached bibliography (Appendix B) which lists recent joint publications of Georgetown and DoD physicians and scientists. I have underlined the names of the DoD participants. While the papers reported do not deal with mammography, but with other topics, we expect this pattern to continue as publications in the clinical aspects digital mammography occur.

### **8.0 SUMMARY:**

During the first year of this research grant we have done a large number of small projects to define the essential parameters for digital mammography to be successful. We believe that our work to date has given us a much better understanding of the parameters necessary for proper image acquisition, image processing and display, and that this preliminary data will allow us to proceed rapidly with the remainder of the project.

This project was focused in defining the characteristics of existing digital mammographic systems and to test their applicability for digital mammography as a replacement for conventional mammography.

#### **9.0 THE ASSIGNED TASKS FOR THIS PROJECT ARE:**

1. *Evaluate the current status of existing digital mammography systems for direct digital mammography and film digitization.*

This is well underway with major factors defined.

2. *Develop a strategy for the optimization of these existing systems including optimization of KVP and MAS.*

The optimization method is underway and has demonstrated substantial improvement in image quality in digital mammography.

3. *Compare the accuracy of these existing systems to conventional screen film systems if the systems appear to be adequate replacements for existing screen film systems using ROC methodology.*

Using three mammographic phantoms initial comparisons have been performed. Clinical tests await further improvements in technology and will be conducted in 1995. Once the system is felt to be of sufficient quality, ROC studies will be performed. Radiologists from Georgetown, MAMC and BAMC will be involved in the ROC studies.

4. *Provide recommendations about how these systems could be implemented to replace existing screen film mammography:*

These recommendations will depend on further investigations. Data for the final implementation report are being gathered. Additional data is needed prior to recommending the best method for implementation. The results of all experiments will be incorporated into an implementation document that will be available at the conclusion of the contract.

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## **APPENDICES:**

- A. BRIEF SUMMARY OF EXPERIMENTS PERFORMED
- B. LIST OF COLLABORATIVE ARTICLES WITH DOD PHYSICIANS AND SCIENTISTS

### **APPENDIX A: BRIEF SUMMARY OF EXPERIMENTS PERFORMED:**

#### **EXPERIMENTAL PHANTOMS USED:**

1. RMI 156 PHANTOM: This phantom is used for certification procedures of the American College of Radiology. It contains fibers, aluminum oxide flecks and small masses.
2. The Nuclear Associates Round Phantom: This is an older mammography phantom containing microcalcification clusters and fibers of different widths.
3. The CIRS square detail phantom: This contains Aluminum oxide and calcium fleck clusters, small masses, and fibers.
4. The CIRS hemicircular phantom: This contains the same objects as #3, but can be used to test for different radiodensity breast composition (fatty vs water radiodensity)
5. The Nuclear Associates CDMAM Phantom: This consists of a series of electroplated gold disks of different diameters and thicknesses. These disks are placed in a non memorizable distribution of positions. This is a very sensitive contrast detail phantom, but its structure interacts with the Fuji RN-3 unsharp masking method producing distorted images.

#### **THE EXPERIMENTS:**

- I. Experiments related to use of magnification onto 200 micron pixel (Fuji ST-3 imaging plates) and onto 170 micron pixels (AGFA experimental imaging plates):

A. Direct geometric magnification of RMI mammography phantom, Nuclear Associates Round phantom and CIRS phantoms.

Magnification factors: 1.5, 1.7, 2.0.

Image processing: Fuji standard and AGFA standard processing with optimization of image processing settings based on appearance of image on workstation monitor.

Findings: One can see most small objects if one uses pixel size approximately 1/2 of nominal size of object desired to be seen. It is possible with 2 x magnification and with proper image processing to see all objects on RMI phantom used for ACR certification at same exposure used for non-magnified image on screen film system. This system is limited to a 4 x 6 inch field of view, but can exceed visibility of screen film systems and exceed resolution requirements for ACR certification.

B. Effect of KVP changes in decreasing total exposure required to make an image. Demonstrated that by increasing exposure to 32 KVP that one could decrease exposure (in mR) to 1/3 that of standard screen film exposure and still show the same information in the Round phantom, which is one that contains calcium flecks. This effect could not be

reproduced in the RMI phantom possibly because the RMI phantom uses aluminum flecks rather than calcium flecks and the KVP affects the absorption of calcium and aluminum differently. The decreased exposure was probably related to the increased sensitivity of the Fuji ST-3 imaging plates.

Increasing the KVP to 36 resulted in images inferior to those of screen film since one could not correct for the contrast changes caused by the higher KVP by available image processing techniques.

#### Significance:

1. Using direct magnification onto a higher sensitivity receptor can improve detectability of objects compared to standard screen film mammography such that one can decrease required exposure.
2. Increasing KVP may provide a method of decreasing patient exposure using the image processing possible with digital information to restore the contrast lost with increased KVP.
3. Image processing can only correct part of the changes occurring with increased KVP. There is a limited range in which this correction is possible with existing image processing software.

C. Images made of breast biopsy specimens testing different methods of image processing:

Five breast biopsy specimens were radiographed using 1.7 X magnification onto a Fuji ST-3 imaging plate. These images were then subjected to a systematic pattern of image processing methods to look for enhancement of breast microcalcifications. Selected combinations of GA, GT, GS, GC, RN, and RE factors were tested to gather preliminary data for optimization of image processing for digital mammography.

#### Findings:

1. Exposure factors are important in that the settings that best demonstrate the calcifications also accentuate the appearance of noise: underexposed images can be "smoothed" using RT factors only with probable loss of information about microcalcifications.
2. Adjustment of the GS and GA factors to produce a pseudo threshold appearance for microcalcifications so that the calcifications are white against an almost black background were very attractive. This proved to be a clinically inapplicable method because it relied on there being a relatively homogeneous fatty background to the calcifications. In a breast with more tissue structure, this thresholding did not produce satisfactory images.

D. Magnification of specific lesions in women for clinical indications. The methods described above were used in two women in whom the greater visibility of microcalcifications possible on digital methods was considered to be clinically important. These were not research cases, but clinical cases. In one case the system demonstrated with greater certainty than screen film small microcalcifications in a lesion that on biopsy proved to be a fibroadenoma. The second case demonstrated that the calcifications were skin calcifications and did not require biopsy. In both cases, the calcifications were more

easily seen on the magnification digital views than on screen film magnification views due to the image processing that could be done.

## II. EXPERIMENTS ON FILM DIGITIZATION OF MAMMOGRAMS:

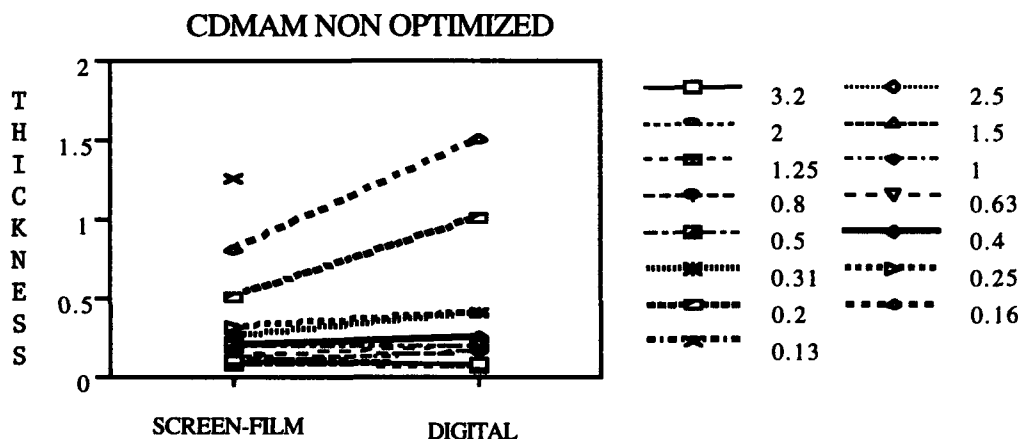
A. Film digitization at 200 microns: 5 mammograms containing calcifications were digitized using a Dupont laser film digitizer. While the presence of calcifications in all five mammograms could be seen to be present, fewer calcifications could be seen and the detectability of shape was less on the digitized mammograms displayed on an ATT Comview workstation than on the original images.

B. Film digitization at 35 microns: Using a 35 micron prototype film digitizer in the offices of DBA Inc. a series of 10 mammograms containing calcifications were digitized. These were viewed on their workstation as magnified sections of images and were compared to direct geometric magnification mammograms of the same regions of microcalcification. We were able to demonstrate to those present that with electronic magnification that the calcifications could be seen on the workstation at least as well as on the geometric direct magnification views. Currently we have been unable to create adequate hard copies of these images to do a formal test of whether or not electronic magnification is a viable replacement for screen film direct geometrical magnification views. Since we currently call back approximately 1 of every 50 patients for direct geometric magnification views, we see the potential of this method for decreasing call backs and the patient anxiety associated with them as being important for further research. We should have this film digitizer on site early in 1994.

## III. EXPERIMENTS IN IMAGE PROCESSING:

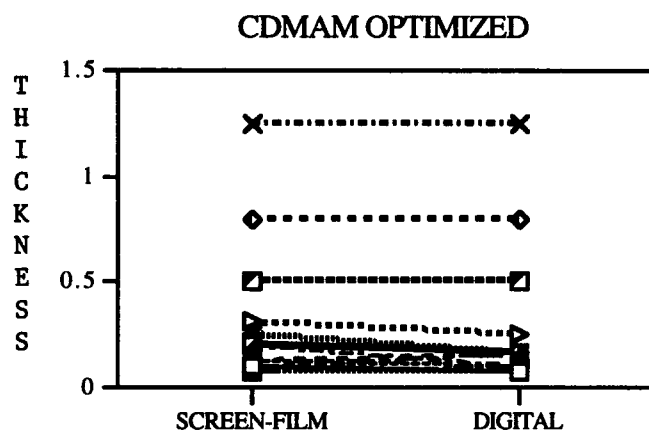
In September of 1993, we received the Fuji Mammography attachment for their storage phosphor imaging system. This is the only FDA approved digital mammography system.

A. We did tests of the system on the RMI, CIRS, and CDMAM Phantoms and found that using the system with the image processing parameters recommended by Fuji on all three phantoms that the images were inferior to conventional screen film systems. Our initial tests from the CDMAM phantom are shown in the following graph which demonstrates that for all smaller objects, the system either did not see the object or required that for a given diameter that the object be thicker.



B. Tests of line pair high contrast resolution: Tests using a standard Nuclear Associates line pair phantom demonstrated that the system could only provide 4.5 lp/mm instead of the 5.0 lp/mm that it should meet according to specifications. Fuji was contacted and asked to make certain that the system was performing satisfactorily. After their check, optimization procedures for image processing were undertaken.

C. Tests after multiparameter optimization: Tests after the multiparameter optimization procedures (which are described below) show that for the CDMAM phantom, that following optimization, the system performed equivalently to screen film images.

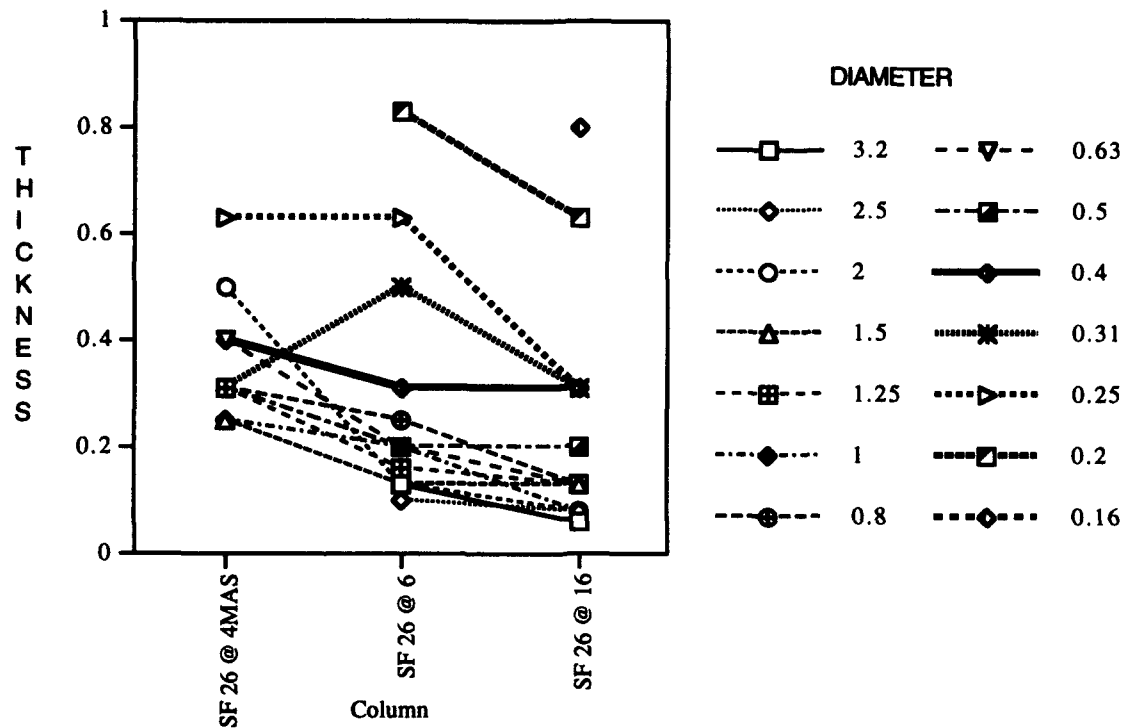


#### IV. Multiparameter optimization:

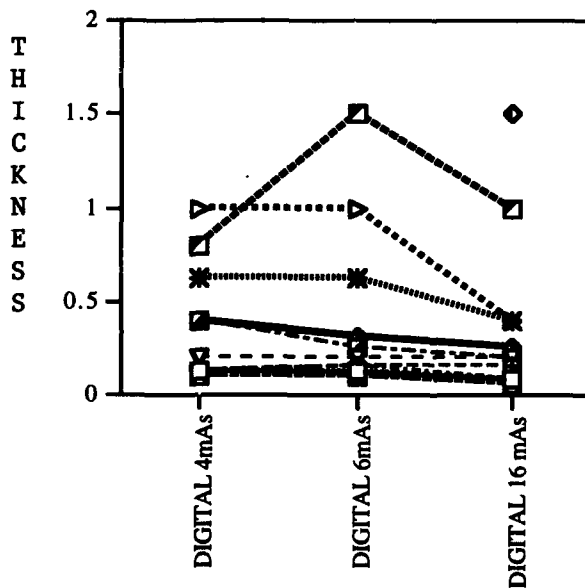
##### A. Exposure tests:

1. Images of the CDMAM phantom were obtained on screen film and Fuji HR-V imaging plates at 26 KVP at 4, 5, 6, 7, 8, 9, 10, 12, 16, 19, 20 MAS and were individually scored. These tests demonstrated that at 4 mAs, the digital system performed better than the screen film system. At all exposures 6 mAs or greater, the screen film system performed better. The screen film system appeared to reach a maximal value at 12 mAs, while the digital system continued to show slight improvement with each increase in exposure.

# SCREEN FILM AT 4, 6, 16 mAs



This chart demonstrates that with increasing exposures in the screen film system, the disks on the CDMAM phantom could be seen both thinner and with smaller diameters as exposure increased from 4 to 6 to 16 mAs.



This chart shows for the digital system, that increased exposure between 4 to 6 mAs had little effect on detection. Increases to 16 mAs showed improved resolution with a smaller object seen and with thinner objects seen.

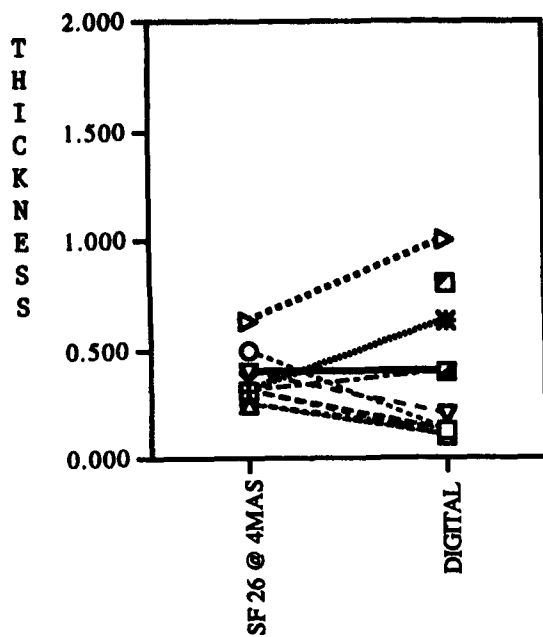


Chart: 4 mAs, screen film and digital. The screen film (SF) system performs better for some objects sizes and less well for others when compared to the digital system. The digital system shows one object (0.2 mm) that is smaller than those seen with the screen film system.

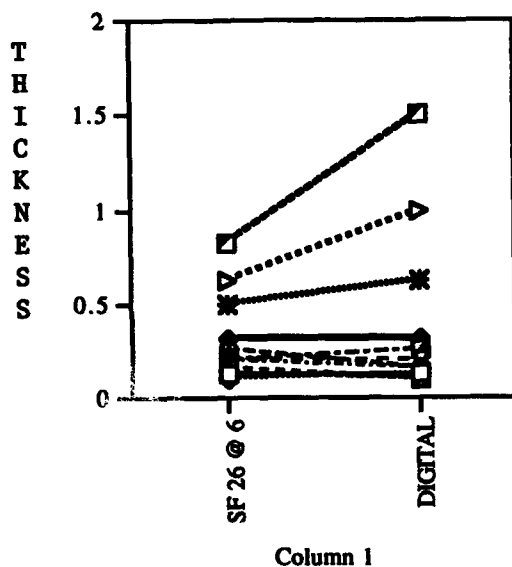


Chart: 6 mAs screen film and digital. At six mAs screen film (SF) shows thinner objects for each object diameter.

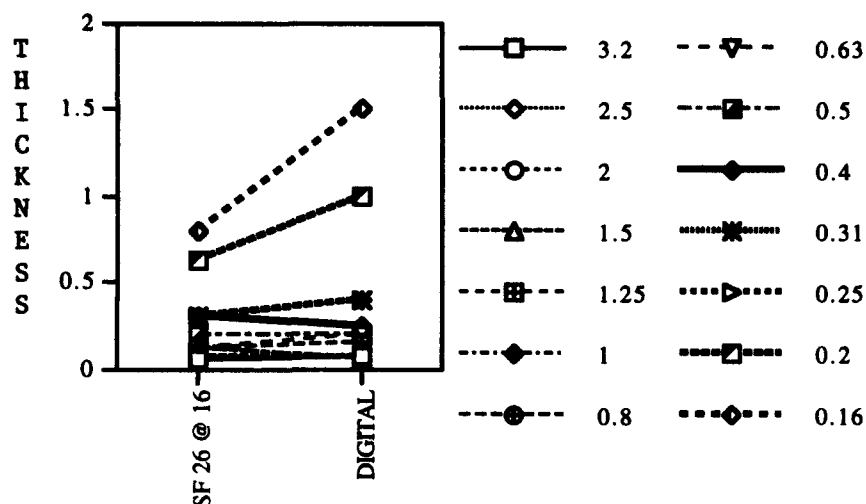


Chart: at 16 mAs, the screen film system shows thinner objects for all object sizes than does the digital system. At 16 mAs, both systems showed the 0.16 mm diameter object. This object could not be seen with 4 or 6 mAs.

These charts demonstrates that the digital system performs better for only the lowest exposure level with the image processing settings used. At higher exposures, the screen film system performed better. These results were obtained as part of the multiparameter optimization procedure and the image processing optimization method had not yet been applied to these images.

2. Measurement of number of mammograms that had exposure levels estimated to be less than 6 mAs. 20 mammograms with proven cancer were measured to determine the optical density of the image in the region of the cancer. The optical density of these images were compared to the optical density of the phantom images done on screen film to determine an estimate of the frequency with which the digital system might yield an advantage. Only one of the 20 cases had an optical density in this region.

3. Comparison of optical density on these 20 breast cancer cases to the characteristic curve of the screen film system used. This test demonstrated that the one case that fell within the range in where the digital system was better was in the optical density range of the toe of the characteristic contrast curve of the screen film system.

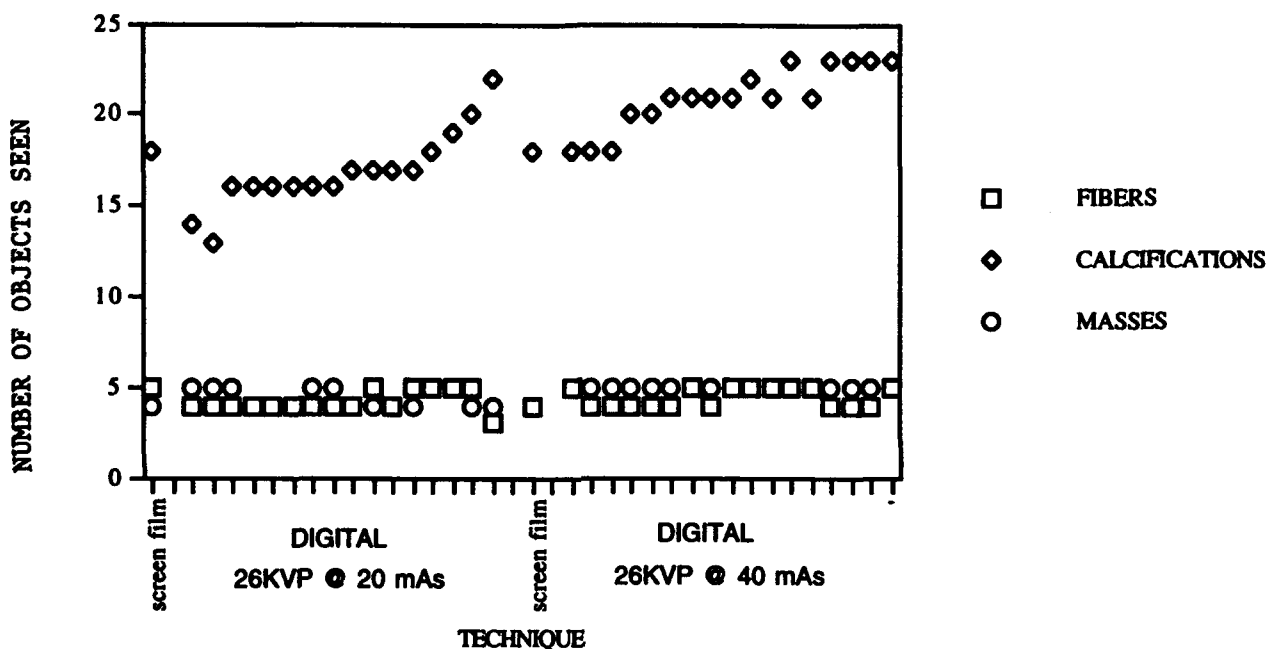
4. Measurements of the effect of optical density of the digital image on the demonstration of features. The digital system allows images to be printed on laser images at various optical densities. This demonstrated that images made in the estimated region of the toe of the laser film characteristic curve had a lower detectability of objects than those made in the steep portion of the curve. These values had to be estimated because of the non uniformity of the images secondary to the heel effect of the mammographic x-ray tube. Digital systems, based on their inherent image analysis methods, exaggerate the heel effect of x-ray tubes.

B. KVP effects: These had been previously studied using Fuji ST-3 imaging plates. Only 2 energies have been tested so far on the HR-V imaging plates: 26 and 36 KVP. On the CDMAM phantom, 26 KVP was better than 36 KVP. These tests were stopped because the dosimeter/KVP meter being used to check machine settings failed during the tests and

had to be returned to the factory for repair. These tests will be completed when the machine is returned.

C. Contrast effects: The effects of increasing contrast on the detectability of the objects in the RMI phantom was tested. Increasing the contrast of the digital image improves the detectability of objects.

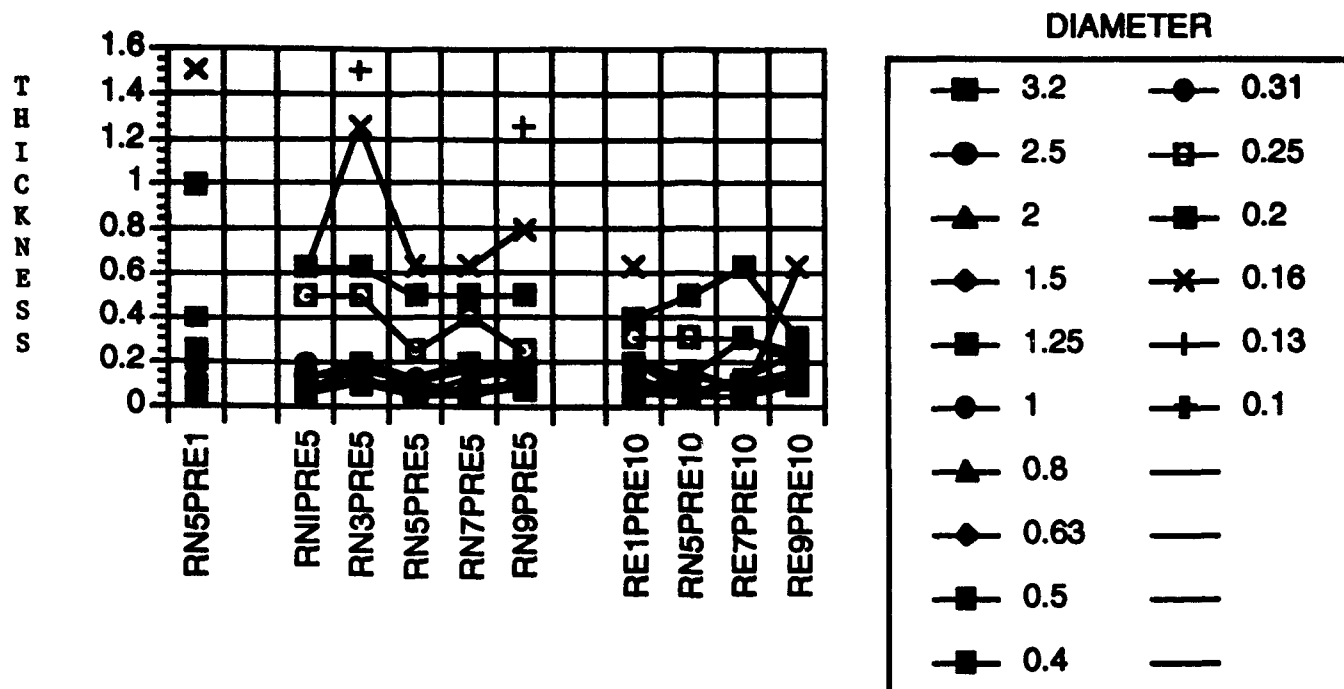
D. Effect of Exposure: As shown in the attached graph, doubling the exposure from 20 to 40 mAs on the digital system improves the detectability of small objects on the RMI phantom. Doubling the mAs on the screen film system has no effect on detectability of objects. The various items under the digital category reflect different image processing settings of RN and RE.



On this chart, the data of the digital sections is based on 16 different RN and RE combination. This chart demonstrates that for each exposure setting 26 KVP at 20 and at 40 mAs, that the screen film system equalled the results of digital for certain types of image processing, but that with other image processing, the visibility of microcalcifications was better with the digital system. The higher exposure with appropriate image processing, resulted in more microcalcifications being seen than were seen with screen film images. The higher exposure resulted in more calcifications being seen with the digital system for most image processing settings used.

E. Effect of spatial frequency filtering: There are two factors that affect spatial frequency filtering: the kernel size and the intensity of enhancement. Using the RMI, CIRS, and CDMAM phantoms, tests were performed using all possible combinations of Fuji RN factors of 1, 3, 5, 7, and 9 and RE factors 0, 2, 5, and 10 as well as selected RE factors of 1 and 16. Results in phantoms demonstrated that low RN combined with high RE improved the detectability of small nodules and that high RN combined with high RE increased the detectability of small calcifications or aluminum flecks. The high RN and RE combination also resulted in an increased visibility of noise which can simulate small calcium flecks.





This graph demonstrates that with increasing spatial frequency filtering intensity (demonstrated as increased RE factors), objects could be detected at thinner diameters. However, at the highest intensity (RE = 10), the smallest objects (0.13 mm) could not be detected, most likely due to the exaggeration of noise which simulated small calcium like densities.

F. Tests of image processing on actual digital mammograms. Digital mammograms done for clinical indications have been stored in our system. The image processing factors that appeared potentially promising on tests on phantoms were then tested on the stored digital mammogram images from two women. These demonstrated that the low RN factors (the ones that increased the detectability of small masses) resulted in distorted images of the other aspects of breast anatomy and resulted in images that radiologists would likely consider unacceptable, especially if combined with higher RE factors. High RN combined with high RE settings resulted in images that appeared likely to be unacceptable as well. The optimal settings of RN 7 or 9 and RE 5, resulted in images that are likely to be considered clinically acceptable by radiologists and equal the diagnostic accuracy of screen film systems when tested on several available breast phantoms.

## **APPENDIX B: LIST OF COLLABORATIVE ARTICLES WITH DOD PHYSICIANS AND SCIENTISTS**

In this list, the DoD physicians' and scientists' names have been underlined. While these articles are not related to digital mammography they are placed here to indicate the collaborative nature of our research in digital radiography.

### **PROCEEDINGS/TRANSACTIONS**

1. Mun S K, Freedman M, Gelish A, DeTreville R, Sheehy M, Hanson M, Hill M, Zacharia E, Sullivan M, Sebera C W: Health Care Using High-Bandwidth Communication to Overcome Distance and Time Barriers for the Department of Defense. SPIE Conference, Enabling Technologies for High Bandwidth Applications, Boston, MA (September 10, 1992).
2. Leckie R G, Meyers C, Parker J, Smith D V, Freedman M, Sheehy M R, Cade L, Goeringer E: Evaluation of Traumatic Lateral Cervical Spine Computed Radiography Images: Quality Control Acceptability of Images for Clinical Diagnosis, Hardcopy versus High Resolution Monitors. SPIE: Medical Imaging (1993). Paper 1897-13.
3. Weiser J C, Leckie R G, Freedman M, Smith D V, Cawthon M A, Romlein J R, Willis C E: Significance of the Fuji AC 1 CR Algorithms on Hardcopy Images. SPIE: Medical Imaging (February 1993). Paper 1897-21.
4. Freedman M, Mun S K, Pe E, Weiser J C, Romlein J R, Lo S-C B, Nelson M: Quality Control of Storage Phosphor Imaging Devices. CAR 93, 7th International Symposium, Berlin (June 24-26, 1993); 456-460 pp.
5. Romlein J, Leckie R, Smith S, Quillin E, Freedman M: Evaluation of Specific PACS Equipment Components - Operational and Maintenance Experience. SPIE: Medical Imaging (February 1994). Paper 2164-19.
6. Leckie R, Ursone R, Willis C, Freedman M: A Basic Teaching Tool For Understanding the Fuji CR Algorithms. SPIE: Medical Imaging (February 1994). Paper 2165-76.
7. Leckie R, Ursone R, Weiser J C, Donnelly J, Norton G, Pe E, Freedman M: Visual comparison of CR Image Quality Based on Different Exposure Techniques. SPIE: Medical Imaging (February 1994). Paper 2165-77.

### **ABSTRACTS**

1. Leckie R G, Freedman M, Weiser J, Willis C, Norton R T, Pe E: Comparison of Computed Radiography Image Quality Based on Different Exposure Techniques. Radiology (1993); 189P:215.

2. Leckie R G, Ursone R L, Freedman M, Donnelly J, Pe E, Norton G: Visual Comparison of Computed Radiographic Image Quality Based on Different Exposure Techniques (abstract). Radiology (1993); 189P:410.
3. Leckie R G, Freedman M, Willis C, Weiser J C, Smith D V, Cawthon M A: Basic Clinical Principles of Computed Radiography for the Radiologist (abstract). Radiology (1993); 189P:415.